Remarks

Claims 1, 2 and 7-12 were pending in the subject application. By this Amendment, the applicants have amended claims 1 and 7 and have canceled claims 2 and 8-12. The applicants have also added new claims 13 and 14. No new matter has been added by these amendments and new claims. Accordingly, claims 1, 7, 13 and 14 are before the Examiner for consideration.

Amendments to the specification and abstract have also been made. No new matter has been added by these amendments.

The amendments to the claims have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. These amendments should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Initially, the applicants hereby reaffirm their provisional election to prosecute the invention of Group I, claims 1, 2, 7 and 8 made by the undersigned during a telephone conversation on August 23, 2006. Thus, claims 9-12 have been cancelled.

The disclosure has been objected to because of informalities. The Office Action states that the application contains sequence disclosures that are encompassed by the definition for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2) but fails to comply with the requirements of 37 CFR 1.821 – 1.825. Specifically, the Office Action states that the amino acid sequences recited in claims 1, 7 and the abstract are not accompanied by the required reference to the relevant SEQ ID number. The applicants appreciate the Examiner's observations and have amended the claims herein to refer to SEQ ID NO:2. The applicants are also submitting herewith a Replacement Sheet for Figure 1 and a new Sequence Listing.

The abstract has also been objected to because of informalities. The applicants have amended the Abstract herein. The applicants respectfully submit that the abstract is in narrative form and is limited to a single paragraph.

The disclosure has also been objected to because there was no "Brief Description of the Drawings" section. This section has been added by this Amendment.

Claims 1 and 7 have been objected to because the acronym "NP-1" was not spelled out. Claims 1 and 7 have been amended as suggested by the Examiner to spell out "neuropilin-1." Accordingly, the applicants respectfully request reconsideration and withdrawal of this objection.

Claims 1 and 2 have been rejected under 35 USC §101 as being directed to non-statutory subject matter. Claim 1 has been amended herein, in accordance with the Examiner's helpful suggestion, to recite that the claimed peptide has been "isolated." Claim 2 has been cancelled herein. Accordingly, the applicant requests the withdrawal of the rejection of claims 1 and 2 under 35 USC §101.

Claims 1, 2, 7 and 8 have been rejected under 35 USC §112, first paragraph, as being non-enabled. The applicants respectfully traverse this ground for rejection because the skilled artisan could readily, and without undue experimentation, practice the full scope of the claims as presently amended.

Please note that the claims have been amended herein to recite that the claimed peptides are in bicyclic form. This limitation significantly limits the number of "fragments" that are encompassed by the claims. In this regard, it can be seen that the given sequence has four cysteine residues and they must be present in order for the peptide to be in bicyclic form. Accordingly, the minimum size of the claimed peptide is only six amino acids less than the given sequence. The applicants respectfully submit that there is a high likelihood that these bicyclic peptides will have substantially the same activity as that for which evidence is presented. Certainly, it would be very straightforward for the highly skilled artisan to test this limited number of peptides, as described in the subject application, to confirm their neuroplin-1 antagonist activity.

It should be noted that the requirement for some experimentation and/or screening does not necessarily make a claim non-enabled. "Enablement is not precluded by the necessity for some experimentation such as routine screening. . . A considerable amount of experimentation is permissible, if it is merely routine . . ." (emphasis added). *In re Wands,* 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988). In the current case, there would not even be a "considerable amount" of testing in view of the very limited number of peptides encompassed by the claims.

It is further noted that the sheer number of compounds which may fall within the scope of a claim is not determinative of the enablement of the specification. See, e.g., *In re Angstadt*, 537 F.2d 498, 190 USPQ 214 (CCPA 1976), where the court observed that a large but finite list of materials, in combination with a teaching of how to carry out the invention, was enabling for purposes of §112. Again, please note that, because of the recitation of "bicyclic" in the current claims, the number of peptides covered is not only "finite," it is actually very limited.

Therefore, the claims as amended are fully enabled even in accordance with the relatively stringent articulation of the enablement standard as set forth at Paragraphs 17-21 of the outstanding Office Action. Please also note that the claims have been amended herein, in accordance with the Examiner's suggestion, to remove reference to "pharmaceutical." Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 USC §112 for lack of enablement.

Claims 1, 2, 7 and 8 have been rejected under 35 USC §112, first paragraph, for failing to comply with the written description requirement. The applicants respectfully traverse this ground for rejection and submit that the claims, as amended, contain only subject matter that is described in the specification in such a way as to clearly convey to one skilled in the art that the inventors had full possession of the claimed invention.

Consistent with the Examiner's articulation of the "written description" requirement as set forth in Paragraph 24 (top of page 14) of the outstanding Office Action, the claims, as amended herein, recite both a biological activity (neuropilin-1 antagonist activity) as well as a conserved structure (bicyclic and having at least 22 of the 28 amino acids of SEQ ID NO:2).

Furthermore, the specification, as filed, provides evidence of the applicants' possession of the invention as now claimed. In this regard, please see, for example, page 2 lines 31-32 wherein the applicants state that "[a] peptide of this invention preferably has 4 Cys residues. It is preferably bicyclic." Accordingly, the applicants respectfully request reconsideration and withdrawal of the written description rejection under 35 USC §112, first paragraph, because these claims, as presently amended, fully comply with this requirement.

Claim 8 has been rejected under 35 USC §112, second paragraph, for insufficient antecedent basis. Claim 8 has been cancelled herein, thereby rendering moot this ground for rejection.

Claims 1, 2, 7 and 8 have been rejected under 35 USC §103(a) as being unpatentable over Li and Kagen (International Publication No. WO 2001/85157-A1) (hereinafter "Li") in view of Achen *et al.*, U.S. Patent Application Publication No. US 2002/0065218 A1) (hereinafter "Achen"). The applicants respectfully traverse this ground for rejection because the cited references, either taken alone or in combination, do not disclose or suggest the particular advantageous peptides claimed by the current applicants.

The Office Action states that Li teaches a linear protein fragment that is identical to the claimed sequence. However, nothing in the Li reference would lead a person of skill in the art to the particular advantageous fragment of the Li sequences that is claimed by the current applicants. As the Office Action states, "[t]he art recognizes that function cannot be predicted from structure alone." (Office Action page 22, Paragraph 19). Because of the unpredictability of identifying active fragments of a sequence, the claimed isolated peptide, which has advantageous neuropilin-1 antagonist activity, would not be rendered obvious by the disclosure by Li of much larger sequences.

An assertion of obviousness without the required suggestion or expectation of success in the prior art is tantamount to using applicants' disclosure to reconstruct the prior art to arrive at the subject invention. Hindsight reconstruction of the prior art cannot support a §103 rejection, as was specifically recognized by the CCPA in *In re Sponnoble*, 56 CCPA 823, 160 USPQ 237, 243 (1969):

> The Court must be ever alert not to read obviousness into an invention on the basis of the applicant's own statements; that is we must review the prior art without reading into that art appellant's teachings. *In re Murray*, 46 CCPA 905, 268 F.2d 226, 112 USPQ 364 (1959); *In re Sprock*, 49 CCPA 1039, 301 F.2d 686, 133 USPQ 360 (1962). The issue, then, is whether the teachings of the prior art would, <u>in and of themselves and without the benefits of appellant's disclosure</u>, make the invention as a whole, obvious. *In re Leonor*, 55 CCPA 1198, 395 F.2d 801, 158 USPQ 20 (1968). (Emphasis in original)

Achen does not add any disclosure that would aid a person of skill in identifying the claimed peptide from the sequences taught by Li. Thus, the Achen reference does not cure the aforementioned defects of the primary Li reference.

As the CAFC has established, an invention will not be rendered obvious merely by combining teachings found in the prior art. *ACS Hospital Systems, Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984). There must be some suggestion or incentive in the prior art to make the combination. *Id.* Also, the prior art must suggest that this combination would have a reasonable likelihood of success. *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). The suggestion to make the combination and likely success may not be gleaned from the applicant's disclosure. *Id.*

The cited art provides no teaching or suggestion of the specific advantageous bicyclic peptides claimed by the current applicants. Therefore, the combination of Li and Achen does not render obvious the subject matter of the applicants' claims. Accordingly, the applicants request the withdrawal of the rejection under 35 USC §103(a).

In view of the foregoing remarks and the amendment above, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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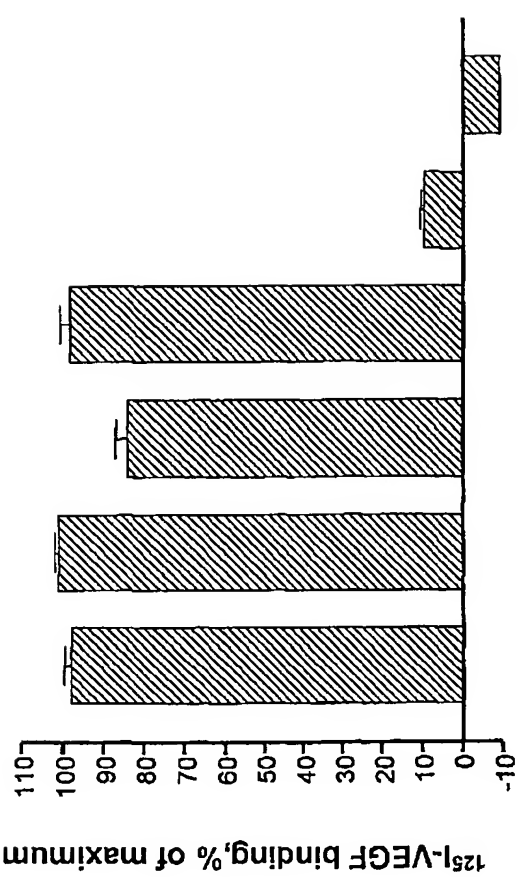
DRS/mdl-la

Attachments: Replacement Sheet for Fig. 1
Annotated Sheet for Fig. 1 showing changes
Substitute Sequence Listing (paper and disk)

Fig. 1.



3283, cyclo $VEGF_{189}$ (152-163) mutant: CVQDPQTOKOSC (SEQ ID NO:3)
3284, cyclo $VEGF_{189}$ (154-161) mutant: CDPQTOKC (SEQ ID NO:4)
3285, cyclo $VEGF_{189}$ (152-163) mutant: YCVQDPQTOKOSCY (SEQ ID NO:5)
3286, dicyclo $VEGF_{165}$ (111-138): ARQENPCGPC'SERRKHLFVQDPQTCKC'S (SEQ ID NO:6)
3287/F9, dicyclo $VEGF_{165}$ (138-165): SC'KNTDSRCKARQLELNERTC'RCDKPRR (SEQ ID NO:2)
3287/F10, dicyclo $VEGF_{165}$ (138-165): SC'KNTDSRCKARQLELNERTC'RCDKPRR (SEQ ID NO:2)

O = Aminobutyric acid